Ovarian Cancer Screening

Update from the PLCO Cancer Screening Trial

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Screening for Disease

- Intuitively appealing
- Cost-effective for a few diseases
- Controversial for many, e.g. breast cancer screening in women under 50
- Well-established principles guide evaluation of screening procedures

Screening for Disease

- Disease affects quality and quantity of life
- Effective treatment is available
- Disease has an asymptomatic period
- Treatment is more effective in early stage, asymptomatic disease
- Prevalence of the condition justifies screening
- Reasonable tests are available (sensitivity, specificity, cost, acceptability)

Influence of prevalence on screening

Characteristics of screening test

95% sensitive (95% of disease identified by test)

95% specific (95% of positive tests due to disease)

10,000 individuals screened

Performance of the screening test varies depending on prevalence:

very common (5%)

uncommon (0.05%)

Results of Screening

Hypothetical disease # 1			
	# with positive test	# with negative test	Totals
Disease	475	25	500
No disease	475	9,025	9,500

Sensitivity of the test = 95%
Specificity of the test = 95%
Prevalence of the disease = 5% (500/10,000)
Subjects screened = 10,000

Results of Screening

Hypothetical disease # 2			
	# with positive test	# with negative test	Totals
Disease	5	0	5
No disease	500	9,495	9,995

Sensitivity of the test = 95%
Specificity of the test = 95%
Prevalence of the disease = 0.05% (5/10,000)
Subjects screened = 10,000

Bias in Screening:
is detection a good thing?

- Lead time bias: detection does not extend life but patient aware of diagnosis longer
- Length bias: indolent cancers found on screen; aggressive cancers present in the interval between screens
- Overdiagnosis bias: detection of tumors that would never have caused clinical disease

Bias in Screening, cont.

Gold standard eliminates bias:

Randomized clinical trial with mortality as the endpoint

Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial

- Objective: to determine if screening reduces mortality
- 10 U.S. centers including Univ. of Utah
- Ages 55-74 at entry
- Enrollment from 1993-2001

Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial

- 154,942 randomized to intervention (screening) vs. usual care

  76,705 men

  78,237 women

PLCO trial, cont.

- Screening for prostate cancer
  - Digital rectal examination yearly for 4 years
  - PSA yearly for 6 years

PLCO trial, cont.

- Screening for lung cancer
  - PA chest x-ray yearly for 3 years; 6 years in smokers

PLCO trial, cont.

- Screening for colon cancer
  - Flexible sigmoidoscopy at baseline and year 5

PLCO trial, cont.

- Screening for ovarian cancer
  - Ovarian palpation yearly
  - CA-125 yearly for 6 years
  - Transvaginal ultrasound yearly for 4 years

Ovarian Cancer Screening

- Ovarian palpation

  Dropped in 1998: no ovarian cancers detected by this method alone; very high contamination rate

Ovarian Cancer Screening

- 78,237 women
  - 39,115 randomized to intervention arm
  - 4,913 prior oophorectomy—not screened
  - 5,386 refused screening

28,816 women screened with CA-125 and TVU

Screening results—year 1

	TVU +	TVU -	Total
CA-125 +	34	365	399 (1.4%)
CA-125 -	1304	26,803	28,107
Total	1338 (4.7%)	27168	28,506

(Only women undergoing both tests are shown—310 excluded)

Screening Results

- 28,816 women received at least one test
  - 368 had abnormal CA-125 only
  - 1304 had abnormal TVU only
  - 34 had abnormality of both

1706 (5.9%) had at least one abnormal test

Results of Ovarian Screening

- 28,816 screened
- 1706 subjects with abnormal screen
- 570 surgeries (33%)
- 29 neoplasms (5%)
- 9 borderline tumors
- 1 granulosa cell tumor
- 19 invasive epithelial cancers (3.5%)

Results of Ovarian Screening

- Surgeries per invasive cancer 28.5
- Cancer per 1000 screens 0.6

- Positive predictive value 1.2
  (cancers/screen positives x 100)

Results of Ovarian Screening

Stage of neoplasms

9 borderline tumors (low malignant potential)	stage I
1 granulosa tumor	stage I

Results of Ovarian Screening

Stage of malignancies, cont.

19 epithelial cancers

16 ovarian	3 stage I, II
	12 stage III
	1 stage IV
2 fallopian tube	stages II, IV
1 primary peritoneal	stage IIIc

Conclusions

- Ovarian screening is acceptable to subjects
- Most screens are negative
- Positive screens result in many surgeries
- Effect on mortality not yet known
- Data are insufficient to change current screening recommendations:

Conclusions, cont.

"Routine screening for ovarian cancer by ultrasound, the measurement of serum tumor markers, or pelvic examination is not recommended."

U.S. Preventive Services Task Force, 1996